DETAILED ACTION

Response to Arguments

Applicants argue over the 35 USC 103 rejection over Arnsten (Science, Vol. 230; pgs. 1273-1276) in view of Olejnik (US Patent 6,627,210) and Chan-Palay (The Journal of Comparative Neurology, 287: 373-392). Applicants argue that the Chan-Palay reference refutes the position of the previous Office Action that Alzheimer's and Parkinson's have similar pathologies. Applicants point to different statements made in Chan-Palay to argue that Alzheimer's and Parkinson's have different pathologies. In response to the above arguments, it is noted that the statements that Applicants are citing are in the introduction of the article in which the discussion of morphological differences and similarities are highlighted between Parkinson's and Alzheimer's. Further, Chan-Palay studied the morphological alterations in locus ceruleus in Alzheimer's and Parkinson's. The purpose of using the Chan-Palay reference was simply to show that both Alzheimer's and Parkinson's show morphological changes in the locus ceruleus.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Accordingly, the following rejections are maintained.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 11 and 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arnsten et al. (Science, Vol. 230; pgs. 1273-1276) in view of Olejnik et al. (U.S. Patent 6,627,210) and Chan-Palay et al. (The Journal of Comparative Neurology, 287: 373-392).

Arnsten et al. teach that there is a loss of catecholamines (norepinephrine) in Alzheimer's disease and that pharmacological treatments may ameliorate the cognitive deficits (pg. 1274, Col. 1 and 2). Arnsten et al. teach that the α_2-receptor agonist clonidine and adrenergic agonists in general will be helpful for patients with Alzheimer's disease (pg. 1276, Col. 2). It is taught that cell deterioration occurs in the locus ceruleus and in particular the portion innervated by the prefrontal cortex (meeting the limitation of claims 3 and 6; pg. 1276, Col. 2). Arnsten also teaches that effects of clonidine may act through the prefrontal cortex surrounding the principal sulcus (page 1275), of which projections from the prefrontal cortex lead to the VTA as Applicants teach in page 8 of their specification. Accordingly, it deemed obvious that the effects of the drug are treating the neural cells of the brain projecting to or from a region of the brain selected from the locus ceruleus and the VTA (in claim 6).

Arnsten et al. do not teach the administration of brimonidine or the treatment of Parkinson's disease.

Olejnik et al. teach compositions comprised of α_2-receptor agonists as the active ingredient, with the preferred α_2-receptor agonist being briminodine (Col. 5, lines 45-48 and claim 1). Other suitable α_2-receptor agonists include clonidine (Col. 5, line 26).

Chan-Palay et al. teach that the locus ceruleus is an important source of norepinephrine and is shown to be affected in several neurologic disorders, including Parkinson's disease and Alzheimer's disease (pg. 373, first paragraph).

Accordingly, it would be obvious to one having ordinary skill in the art at the time of the invention, to combine the teachings of Arnsten et al, which teaches the treatment potential of an α_2-receptor agonist in Alzheimer's disease and further teaches that the α_2-receptor agonist is having effects on neurons in brain regions projection to or from the locus ceruleus or VTA with the teachings of Olejnik et al. which teach brimonidine as an α_2-receptor agonist. One would be motivated to combine the references with a reasonable expectation of success because of the teaching that an α_2-receptor agonist can treat Alzheimer's disease and clonidine and brimonidine are both α_2-receptor agonists. Further, it would be obvious to that α_2-receptor agonists would beneficially treat Parkinson's disease because of the teachings of Chan-Palay which teaches that the locus ceruleus is involved with disorders such as Parkinson's disease. One would be motivated to treat Parkinson's disease with brimonidine because Chan-Palay teaches that norepinephrine in the locus ceruleus is implicated in Parkinson's and Alzheimer's disease, and Arnsten et al. teach that cell deterioration occurs in the locus ceruleus in Alzheimer's disease and that α_2-receptor agonists in general are a beneficial for treatment; therefore, there is a reasonable expectation of success because both diseases have similar pathologies.

Furthermore, it is obvious to vary and/or optimize the amount of brimonidine provided in the composition, according to the guidance provided by Arnsten and Olejnik, to provide a composition having the desired properties such as the desired concentrations of brimonidine to effectively treat Parkinson's and/or Alzheimer's disease. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is (571)272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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